

Bioterrorism Recognition and Reporting Update on New Reporting Requirements and Training Resources

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Clinical recognition of bioterrorist threat diseases

Health care providers should be alert to diagnostic clues and patterns of illness that might indicate an unusual infectious disease associated with intentional release of a biological agent, and should report any unusual diseases or clusters of illness to their local health department. The agents of highest concern, as defined by the Centers for Disease Control and Prevention (CDC) are *Bacillus anthracis* (anthrax), *Yersinia pestis* (plague), *Variola major* (smallpox), *Clostridium botulinum* toxin (botulism), *Francisella tularensis* (tularemia), and the hemorrhagic fever viruses (e.g., Ebola, Lassa, Marburg). In California, brucellosis has been included in this high-priority group. These agents have the potential to be used as weapons, based on ease of dissemination or transmission, potential for major public health impact (e.g., high mortality), potential for public panic and social disruption, and requirements for public health preparedness such as antibiotic and vaccine stockpiling. The following summary of the clinical features of these diseases was adapted from the October 19, 2001 edition of the Morbidity and Mortality Weekly Report (www.cdc.gov/mmwr/preview/mmwrhtml/mm5041a2.htm) and other resources listed at the end of this article.

Anthrax: Nonspecific prodromal symptoms of **inhalational anthrax** include fever, malaise, headache, myalgias, non-productive cough, and chest discomfort. Nausea or abdominal pain may be present. Approximately 2-4 days after initial symptoms, sometimes after a brief period of improvement, respiratory failure and hemodynamic collapse ensue. Meningitis and altered mental status may also occur. A widened mediastinum and/or pleural effusion may be seen on chest radiograph. Gram-positive bacilli may be cultured from blood or cerebrospinal fluid, usually 2-3 days after onset of illness. Cutaneous anthrax follows deposition of the organism onto the skin, occurring particularly on exposed areas of the hands, arms, or face. A pruritic macule or papule enlarges and ulcerates after 1-2 days. Small, 1-3 mm satellite vesicles may surround the ulcer. The ulcer develops a painless, depressed, black eschar, usually with surrounding local edema. Lymphangitis, tender lymphadenopathy, and systemic symptoms of fever, malaise, or headache may also occur.

Plague: Clinical features of pneumonic plague include fever, cough with mucopurulent sputum (gram-negative rods may be seen on gram stain), hemoptysis, and chest pain. A chest radiograph will show evidence of bronchopneumonia.

Botulism: Clinical features include symmetric cranial neuropathies (e.g., drooping eyelids, blurred vision, difficulty swallowing or speaking) followed by symmetric descending weakness and respiratory failure from respiratory muscle paralysis. No sensory deficits are present. Inhalational botulism that may occur from an intentional aerosol release of botulinum toxin would have a similar clinical presentation as foodborne botulism, but the gastrointestinal symptoms that accompany foodborne botulism may be absent.

Smallpox (variola): The acute clinical symptoms of smallpox resemble other acute viral illnesses, such as influenza, beginning with a 2-4 day nonspecific prodrome of fever, malaise, prostration, cough, headache, and backache before onset of a rash. The lesions of the rash begin as small macules, progress to firm papules, then vesicles, which are usually multiloculated and soon become opaque and pustular. The vesicles are typically raised and firm to the touch, and 8 to 9 days after onset of the rash, they become pit-like and dimpled. Varicella (chickenpox) may be differentiated from smallpox by the distribution and evolution of the rash. The rash of varicella is most prominent on the trunk and develops in successive groups of lesions over several days, resulting in lesions in various stages of development and resolution. In comparison, the rash of smallpox is typically most prominent on the face and distal extremities, and lesions on any one part of the body are at the same stage of development.

Inhalational tularemia: Inhalation of *F. tularensis* causes an abrupt onset of an acute, nonspecific febrile illness beginning 3-5 days after exposure, with pleuropneumonitis developing in a substantial proportion of cases during subsequent days.

Hemorrhagic fever (e.g., illness caused by Ebola or Marburg viruses) After an incubation period of usually 5-10 days (range: 2-19 days), illness is characterized by abrupt onset of fever, myalgia, and headache. Other signs and symptoms include nausea and vomiting, abdominal pain, diarrhea, chest pain, cough, and pharyngitis. A maculopapular rash, prominent on the trunk, develops in most patients approximately 5 days after onset of illness. Bleeding manifestations, such as petechiae, ecchymoses, and hemorrhages, occur as the disease progresses.

Brucellosis: The insidious onset of irregular fever, chills, malaise, headache, profound fatigue, weakness, and weight loss occurs from 5-60 days after exposure. Musculoskeletal manifestations include arthralgias, sacroiliitis, and paravertebral abscesses. Anorexia, nausea, vomiting, diarrhea, and hepatosplenomegaly may be seen. Cough and pleuritic chest pain may occur. The organism is a tiny, slow-growing, gram-negative coccobacillus that may be isolated in blood or bone marrow culture. Anemia and thrombocytopenia are possible, and chest radiograph findings are variable (bronchopneumonia, abscesses, single or military nodules, enlarged hilar nodes, effusions, or no abnormalities).

Unusual patterns of illness: Clinicians should consider the possibility of an intentional release of a biological agent if they observe: a) multiple patients presenting with the same clinical syndrome, clustered in time and/or geography, especially occurring in otherwise healthy individuals (e.g., several persons who work in the same building who present over two or three days with fever, gram-negative pneumonia, and rapid progression to sepsis); b) an unusual age distribution for common diseases (e.g., many cases of chickenpox-like illness among adults might represent misdiagnosed smallpox); c) an unusual seasonal distribution of illness (e.g., an increase in influenza-like illness in the summer, outside of the usual flu transmission season in the Northern Hemisphere).

New reporting requirements

Emergency amendments to the California Code of Regulations concerning reportable diseases and conditions became effective November 5, 2001. The diseases/conditions/agents that pose the

most serious threat for bioterrorism are immediately reportable by health care providers and clinical laboratory directors to the local health department.

The diseases/conditions that health care providers must report *immediately* (including nights, weekends, and holidays) by telephone to the local health department are suspected or confirmed cases of:

- Anthrax
- Botulism
- Brucellosis
- Smallpox (variola)
- Tularemia
- Varicella deaths
- Viral hemorrhagic fevers
- Occurrence of any unusual disease
- Outbreaks of any disease

Health care providers are defined as physicians, surgeons, veterinarians, podiatrists, nurses, nurse practitioners, nurse midwives, school nurses, infection control practitioners, physician assistants, dentists, coroners, and medical examiners. The requirement for laboratories to report these diseases does **not** replace the health care provider's legal obligation to report. More importantly, public health action to find the source and implement preventive treatment should not be delayed until a definitive laboratory diagnosis is reached, which may take several days, depending on the organism. Therefore, health care providers should immediately report even **suspected** cases or conditions to their local health department prior to receiving laboratory confirmation. Detailed information about the amended regulations may be found at the California Department of Health Services Web site, www.dhs.ca.gov/.

Once notified, the local health department will arrange for specialized laboratory testing; provide a guidelines for treatment, prophylaxis, and infection control; begin a public health investigation; and activate local, state, and federal emergency response systems as appropriate.

Selected references and resources

Anthrax

JAMA bioterrorism Web site: clinical case reports, CDC guidelines, and updates on anthrax investigations from the MMWR. <http://pubs.ama-assn.org/bioterr.html>

Jernigan JA, Stephens DS, Ashford DA. Bioterrorism-related inhalational anthrax: the first 10 cases reported in the United States. *Emerging Infectious Diseases*, Nov-Dec 2001; 7(6):933-44. www.cdc.gov/ncidod/eid/vol7no6/jernigan.htm

Inglesby TV, Henderson DA, Bartlett JG. Anthrax as a Biological Weapon, Medical and Public Health Management. *JAMA*, May 12, 1999; 281(18):1735-45. <http://pubs.ama-assn.org/bioterr.html> - anthrax

Botulism

Arnon SS, Schechter R, Inglesby TV. Botulinum Toxin as a Biological Weapon, Medical and Public Health Management. JAMA, February 28, 2001; 285(8):1059-70.
pubs.ama-assn.org/bioterr.html#botulinum

Plague

Inglesby TV, Dennis DT, Henderson DA. Plague as a Biological Weapon, Medical and Public Health Management. JAMA, May 3, 2000; 283(17):2281-90.
pubs.ama-assn.org/bioterr.html#plague

Smallpox

Henderson DA, Inglesby TV, Bartlett JG. Smallpox as a Biological Weapon, Medical and Public Health Management. JAMA, June 9, 1999; 281(22):2127-37.
pubs.ama-assn.org/bioterr.html#smallpox

Fenner F, Henderson DA, Arita I. Smallpox and its eradication. World Health Organization, 1988. [Excellent clinical descriptions and photos, pp.1-68.]
www.who.int/emc/diseases/smallpox/Smallpoxeradication.html

Tularemia

Dennis DT, Inglesby TV, Henderson DA. Tularemia as a Biological Weapon, Medical and Public Health Management. JAMA, June 6, 2001; 285:2763-2773
pubs.ama-assn.org/bioterr.html#tularemia

General bioterrorism resources — clinical and hospital preparedness

CDC Bioterrorism Preparedness and Response Program Web site: fact sheets about chemical and biological agents, training materials, guidelines, and updates on recent anthrax investigations.
www.bt.cdc.gov/

Santa Clara County Public Health Department “Zebra Pack” provides a one-page clinical synopsis (diagnosis, laboratory testing, treatment, prophylaxis) for high-priority bioterrorist threat agents. www.sccphd.org/diseasecontrol/bioterrorism.asp

US Army Medical Research Institute of Infectious Diseases (USAMRIID) Medical Management of Biological Casualties Handbook: concise information on biological agents, diagnosis, treatment, and prophylaxis.
www.nbc-med.org/SiteContent/HomePage/WhatsNew/MedManual/Feb01/handbook.htm

California Hospital Bioterrorism Response Planning Guide: guidelines for hospital preparedness for bioterrorism, including roles of hospital departments, emergency response systems, disease-specific frequently asked questions and home care instructions, and communication plans.
www.dhs.ca.gov/index.htm

Posters and slide sets

Educational poster of bioterrorism clinical syndromes available in PDF, HTML, or Excel formats: www.labt.org/agent_facts/BioterrorismPoster.pdf
www.medept.org/sfdph/bt/syndromes/index.html

Bioterrorism: Are You Prepared?

Slide set for training clinicians on recognition, clinical management, and reporting of bioterrorist threat diseases. www.ph.ucla.edu/cphdr

Bioterrorism: What Every Clinician Should Know

This training slide set covers bioterrorist threat disease recognition and treatment, historical background of bioterrorism, and the interaction of clinicians and public health agencies.

www.labt.org/BT_Grandrounds.asp

Valuable Bioterrorism Updates — www.medbd.ca.gov/

Because of public and professional concerns regarding biological terrorism, the Board has added links on its Web site to the California Department of Health Services (DHS) and Centers for Disease Control and Prevention (CDC) Web sites. This will facilitate ready access to timely information on prevention and response to anthrax and other forms of bioterrorism. Toll-free numbers with recorded non-emergency anthrax-related information are available at the DHS site. Anthrax information and public health emergency preparedness and response are available at the CDC site. Routinely check these sites as the information provided is updated on a daily basis.